

FIGURE 1

Human G Protein-Coupled Receptor Family

(Receptors known as of January, 1999)

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| | | | | |
|-------------------------------------------|----------|-------------------------------------------------|--------------------------------------|-----------------------------------------------------|
| •Thyrotropin | 1 | Thyroid | Endocrine | Thyroidism, Metabolism |
| •Rhodopsin | 1 | | | |
| •Opsin | 5 | | | Ophthalmic Diseases |
| •Olfactory | 4(-1000) | Nose | Smell | Olfactory Diseases |
| •Prostanoid | | | | |
| •Prostaglandin | 5 | Arterial, Gastrointestinal Vessels, Heart, Lung | Vasodilation, Pain Inflammation | Cardiovascular, Analgesic Cancer, Anti-Inflammatory |
| •Lysophosphatidic Acid | 2 | Most Cells | Cell proliferation | Cancer |
| •Sphingosine-1-phosphate | 2 | White Blood Cells, Bronchus | Inflammation | Asthma, Rheumatoid Arthritis |
| •Leukotriene | 1 | Arterial, Gastrointestinal Arterial, Bronchus | Platelet Regulation Vasoconstriction | Cardiovascular, Respiratory |
| •Prostacyclin | 1 | | | Cardiovascular, Respiratory |
| •Thromboxane | 1 | | | Cardiovascular, Respiratory |
| •Nucleotide-like | 4 | Vascular, Bronchus Vascular, Platelets | Multiple Effects Relaxes Muscle | Analgesics, Memory |
| •Adenosine | 4 | Brain | Sensory Perception | Anti-inflammatory, Anti-asthmatic |
| •Purinoreceptors | 4 | Most Peripheral Tissues | Inflammation | |
| •Cytanab | 2 | | | |
| •Platelet activating factor | 1 | | | |
| •Gonadotropin-releasing hormone | 1 | Reproductive Organs, Pituitary Pituitary, Brain | Reproduction Thyroid Regulation | Prostate Cancer, Endometriosis |
| •Thyrotropin-releasing hormone | 1 | Gastrointestinal | Neuroendocrine | Metabolic Regulation |
| •Growth hormone- inhibiting factor | 1 | | | Oncology, Alzheimer's |
| •Melatonin | 1 | Brain, Eye, Pituitary | | Regulation of Circadian Cycle |
| ● Class II | | | | |
| Secretin like | | | | |
| •Secretin | 1 | Gastrointestinal, Heart Bone, Brain | Digestion Calcium Resorption | Obesity, Gastrointestinal Osteoporosis |
| •Calcitonin | 1 | | | |
| •Corticotropin releasing factor/urocortin | 1 | Adrenal, Vascular, Brain Adrenals, Fat Cells | Neuroendocrine Sugar/Fat Metabolism | Stress, Mood, Obesity Diabetes, Obesity |
| •Gastric inhibitory peptide (GIP) | 1 | Liver, Fat Cells, Heart Pancreas, Stomach, Lung | Gluconeogenesis Gluconeogenesis | Cardiovascular |
| •Glucagon | 1 | Brain | Neuroendocrine | Diabetes, Obesity |
| •Glucagon-like Peptide 1 (GLP-1) | 1 | Bone, Kidney | Calcium Regulation | Growth Regulation |
| •Growth hormone-releasing hormone | 1 | Brain, Pancreas, Adrenals | | Osteoporosis |
| •Parathyroid hormone | 1 | | | Metabolic Regulation |
| •PACAP | 1 | | | |
| •Vasoactive intestinal polypeptide (VIP) | 1 | Gastrointestinal | Motility | Gastrointestinal |
| ● Class III | | | | |
| Metabotropic Glutamate | 7 | Brain | Sensory Perception | Hearing, Vision |
| •GABA _A | 1 | Brain | Neurotransmitter | Mood Disorders |
| •Extracellular Calcium Sensing | 1 | Parathyroid, Kidney, GI Tract | Calcium Regulation | Cataracts, GI Tumors |

Figure 2

G protein-coupled receptors:

(Division into Class A
Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533
npivyafrqkfrvtflkiwndhfcq pappidedlp eerpdd
Class A
2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP_000670
npiiyccsskeskfkravrlgcqcrgrrrrrrlrgcaytvpwtrggslerqsqrkdsiddsgscslsgsqrtpsapspgylgrgap
ppvelcapewkapgallspapeppgrghdsgplftklltepespgtdggasngceaaadvangqpgfknsnmlapqgf
Class A
3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447
npviyifnhdfrrafkiklrcgdrkriv
Class A
4. **alpha-2B-adrenergic receptor** - human. ACCESSION A37223
npviytfmqdfrafrilcrpwqtaw
Class A
5. **alpha-2C-adrenergic receptor** - human. ACCESSION A31237
npviytvfndfrpskhhlfrrrrgfrq
Class A
6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP_000675
npiiycrspdfrkafqgllecarraarrhathgdrprascclarpgpppspgaaasddddvvvgatpparlep wagcngaaads
d ssldpcrprgfaseskv
Class A
7. **beta-2 adrenergic receptor**. ACCESSION P07550
npiiycrspdfrfiafqellclrsslkayngyssngntgeqsgyhvqekenklcedlpgtedfvghqgtvpsdnidsqgrncstd
sll
Class A
8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP_000785
npiiyafnadfrkafstlbgcyrlcpatnmaietvsinmngaaamfsshheprgsiskecnlyliphavgssedlkkeeagiarplekl
palsvildydtvslekiqpitqngqht
Class A
9. **D(2) dopamine receptor**. ACCESSION P14416
npiiyttfneirfkafkikhc
Class A
10. **d3 dopamine receptor** - human. ACCESSION G01977

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npviytfniefrkafklkilsc

Class A

11. **dopamine receptor D4** - human. ACCESSION DYHUD4
npviytvfnafnrnfrkalracc
Class A
12. **dopamine receptor D5** - human. ACCESSION DYHUD5
npviyafhadfqkvfaqllgcshfcstrpvtnismelisynqdivfhkeiaayihmmpnavpgnrevdndeeegpfdrmfqi
yqtspdgdpvaesvweldcegeisldkitpftpngfh
Class A
13. **muscarinic acetylcholine receptor M1** [Homo sapiens]. ACCESSION NP_000729
npmcyalcnkafrdtfrllcrwdkrrwrkipkrpgsvhrtprsc
Class A
14. **muscarinic acetylcholine receptor M2** [Homo sapiens]. ACCESSION NP_000730
npacyalcnafatkfkhlilmchyknigatr
Class A
15. **muscarinic acetylcholine receptor M3** [Homo sapiens].
npvcyalenktrttfkmillcqcdkkrrkqqyqqrqsvifhkrapcqal
Class A
16. **muscarinic acetylcholine receptor M4** [Homo sapiens]. ACCESSION NP_000732
npacyalcnafatkfrhlllcqyrmigtar
Class A
17. **m5 muscarinic receptor.** locus HUMACHRM ACCESSION AAA51569
npicyalcntrtkfkmillcrwkkkveeklywqgnsklp
Class A
18. **5-hydroxytryptamine (serotonin) receptor 1A** [Homo sapiens]. ACCESSION BAA90449
npviyafmkdfqnafkkiikcf
Class A
19. **5-hydroxytryptamine (serotonin) receptor 1B** [Homo sapiens]. ACCESSION BAA94455
npiiytmnsnedfkqafhklirfkcts
Class A
20. **5-hydroxytryptamine (serotonin) receptor 1E** [Homo sapiens]. ACCESSION BAA94458
npllytsnedfklaflaklkircre
Class A
21. **OLFACTOORY RECEPTOR 6A1.** ACCESSION O95222

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npiiyclrmqevkralccilhlyqhqdppkgsrnv

Class A

22. **OLFACTORY RECEPTOR 2C1.** ACCESSION O95371

npliythrmmevkgalrllgkgrevg

Class A

23. **angiotensin receptor 1 [Homo sapiens].** ACCESSION NP_033611

nplfygflgkkfkryflqlkyippkakshslnsfkmstlsyprsdnvssstkkpacfeve

Class B

24. **angiotensin receptor 2 [Homo sapiens].** ACCESSION NP_000677

nplflycvgnrffqkklrvsfrvpitwlqkresmcrkssslremetvfs

Class B

25. **interleukin 8 receptor beta (CXCR2) [Homo sapiens].** ACCESSION NM_001557

NPLIYAFIGQKFRHGLLKILAIHGLISKDSLKDPSFVGSSSGHTSTTL

Class B

26. **cx3c chemokine receptor 1 (cx3cr1) (fractalkine receptor)**

ACCESSION P49238

npliyafagekfrrlyhlygkclavlcgrsvhvdfsssesqrslrhgsvlssnftyhtsgdallll

Class B

27. **neurotensin receptor - human.** ACCESSION S29506

n pilynlvsanfrhiflatlaclcpvwffffkrpafsrkadvssnhflssnatretly

Class B

28. **SUBSTANCE-P RECEPTOR (SPR) (NK-1 RECEPTOR) (NK-1R).** ACCESSION P25103

npiiyccndrfrrgkhafrccepfigsagdyeglemkstrylqtqsvykvsllettistvgaheeedpedgpkaftsssdltncssrsdsktmtesfsnnvls

Class B

29. **vasopressin receptor type 2 [Homo sapiens].** ACCESSION AAD16444

npwiyasfssssselrsllcicargrpsslgpqdescftassslakdtss

Class B

30. **thyrotropin-releasing hormone receptor - human.** ACCESSION JN0708

npviynlmsqkfraafrkclcnckqptekpanysvalnsvikesdhfteldditvtdtylsafkvsfddtcleasevsfsqs

Class B

31. **oxytocin receptor - human.** ACCESSION A55493

npwiymflghlfhelvqrflccasaylkgrrlgetaskksnsssfvlshrssssqrscsqpsata

Class B

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32. **neuromedin U receptor 1 [Homo sapiens]**. ACCESSION AAG24793
nlpvlyslmssrfretfqcalclgacchrlprhsshsrsmittgstlcvdvgsgswvhplagndpeaqqtetdps
Class B
33. **gastrin receptor**. ACCESSION AAC37528
nplvycfmhrfrfqacletcarccprpprparpalpdedptpsiaslsrsyttstlpgp
Class B
34. **galanin receptor 3 [Homo sapiens]**. ACCESSION 10879541
nplvyalasrhfrarflwpcgrrrharrallrvpassgppcpgdarpsgrllaggqgpepregpvhggeaarge
Class A
35. **edg-1 - human**. ACCESSION A35300
npiiytltnkemrrafirimsccckpcsgdsagkfkriiagmefsrsksdnsshpkdegdnpetimssgnvnsss
Class A
36. **central cannabinoid receptor [Homo sapiens]**. ACCESSION NP_057167
npiiyalrsksdlrhafsrmpfcsgtaqlndsmgdsdclhkhannaavhraescikstvkiakvtmsvstdsacal
Class A
37. **delta opioid receptor - human**. ACCESSION I38532
nplvyaflenfkrcfrqlcrkpcgrpdpssfsrpreatarervtactpsdggggrraa
Class A
38. **proteinase activated receptor 2 (PAR-2) human**. ACCESSION P55085
dpfvyyfvshdfrdhaknallcrsvrtvkqmqvsltskkhsrksssyssssttvktsy
Class B
39. **vasopressive intestinal peptide receptor (VIPR) rat**. ACCESSION NM_012685
NGEVQAEELRRKWRWRWHLQGVLGWSSKSQHPWGGSNGATCSTQVSMLTRVSPSARR
SSSFQAEVSLV
Class B

Figure 3

A. Human V2R DNA (nucleotides encoding the last 29 amino acids of the V2R and the adjacent stop codon):

gccccgggacgcacccacccagctgggtccccaaagatgagtcctgcaccaccegcagtcct
ccctggccaaggacacttcatcgta

B. PCR amplified human V2R DNA fragment:

gggccgcacggggacgcacccacccagcttgggtccccaaagatgagttctgcacccacgccc
actctctctctgcccaggacactcatcgtaagattccgcgggtttaga

*Additions and changes to the V2R DNA are underlined.

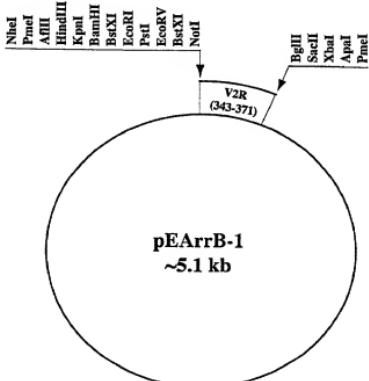
*The Sma I (cccg₄gg) restriction enzyme site (underlined in Fig. 3A) was eliminated in the amplified DNA fragment by changing a cytosine to an adenine.

*A Not I restriction site (gcggccgc) was incorporated into the amplified DNA fragment by adding 6 nucleotides (gcggcc) to the 5' end of the V2R DNA.

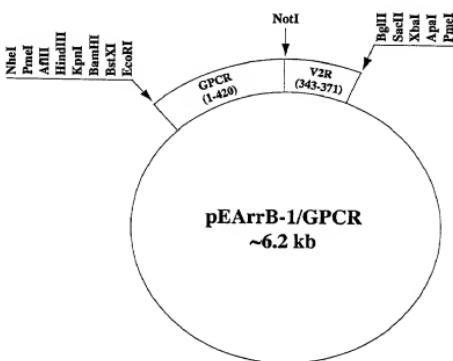
*Bgl II (agatct), Sac II (ccgcgg), and Xba I (tctaga) restriction enzyme sites were added to the 3' end of the V2R DNA.

Figure 4

A.



B.



C.

...AAARGRTPPSLGPQDESCTTASSSLAKDTSS

Figure 5

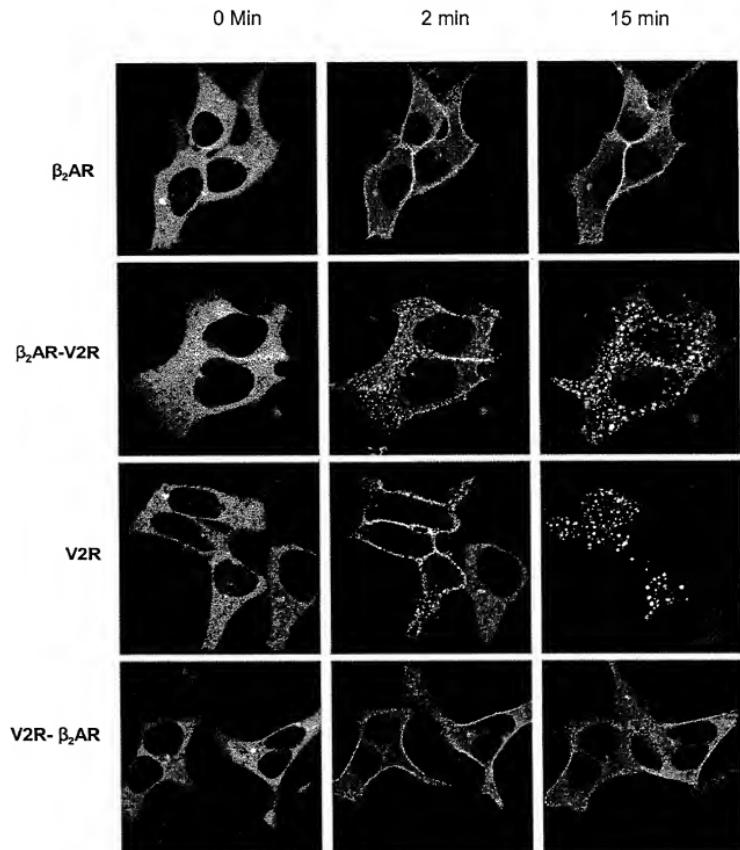


Figure 6

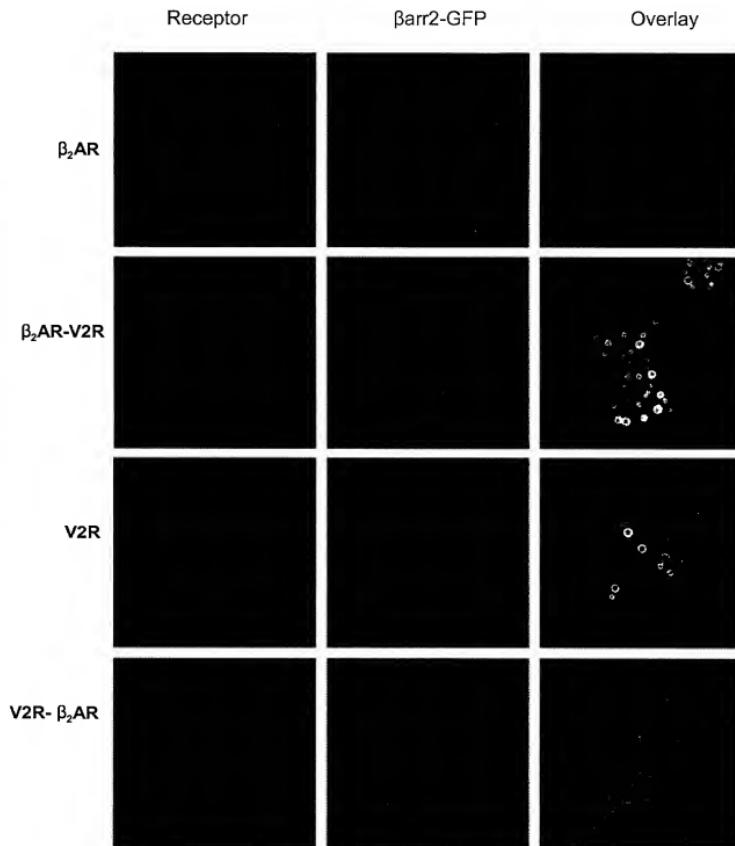


Figure 7

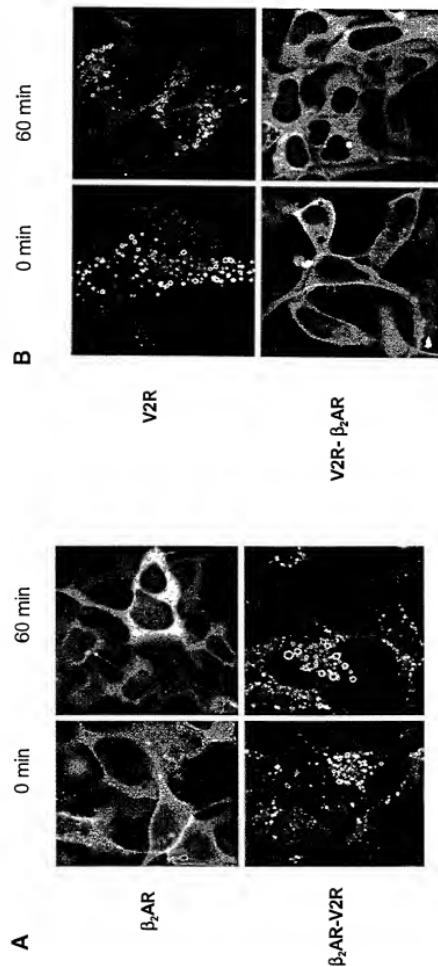


Figure 8

A

1) V2R CARGRTPPSLGPQDESCCTTASSSLAKDTSS
2) V2R-S362X CARGRTPPSLGPQDESCCTTA
3) V2R-SSSTSS/AAAAAA CARGRTPPSLGPQDESCCTTAAAALAKDAAA
4) V2R-TSS/AAA CARGRTPPSLGPQDESCCTTASSSLAKDAAA
5) V24-SSS/AAA CARGRTPPSLGPQDESCCTTAAAALAKDTSS
6) β_2 -AR-V2R-SSS/AAA CARGRTPPSLGPQDESCCTTAAAALAKDTSS
7) β_2 -AR CLRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLEDLP-
8) β_2 -AR413-V2R10 CLRRSSLKAYGNGYSSNGNTGEQSGYHVEQEKENKLLEDLP-
9) B2ar360-V2R10 CLRRSSLKAYGNGYSSNGNTSSLAKDTSS

B

V2R NPWIYASFSSSVSELRSLLCCARGRTPPSLGPQDESCCTTASSSLAKDTSS
AAA-1 -----AAA-----
AAA-2 -----AAA-----

NTR-1 NPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNMSSNHAFSTSATRELY
AMAA -----A-AA-----
AAA -----AAA-----

OTR NPWIYMLFTGHLFHELVQRFLCCSASYLKGRRLGETSASKNSSFVLSHRSSSQRSCSQPSTA
AAAA -----AAA-----
AAA-1 -----AAA-----
AAA-2 -----AAA-----

C

SPR NPIIYCLNDRFRLGFKHAFRCCPFISAGDYEGLEMKSTRYLQTQGVYKVSRLETTISTVGAHEEEPE-
GPKATPSSLKLTNCSSRSDSKTMTESFSSNVLS
383X -----X-----
355X -----X-----
325X -----X-----
AAIAA -----AA-AA-----
AAA -----A-AA-----

Figure 9

Amino Acid Sequence of the Wild-Type Receptors

A. Amino acid sequence of the wild-type V2R

MLMASTTSAVPGHPSLPSNSQERPLDTRDPLLARAELALLSIVFVAVAL
SNGLVLAALARRGRRGHWAPIHVFIGHLCLADIHALVALFQVLPLAWKATDRFR
GPDALCRAVKYLQMVGMYASSYMIAMTLLDRHRAICRPMILAYRHGSAGAHWNRP
VLVVAWFSLLLSPQLFIFQAQRNVEGGSGVTDCWACFAEPWGRRRTYVTWIALM
VFVAPTLGIAACQVLI~~FREI~~HASLVPGP~~SERPG~~RRRTGSPGEGAHVSAA
VAKTVRMTLVIVVVVYVLCWAPFFLVQLWAADPEAPLEGAPFVLLMLIASLNS
CTNPWIYASFSSSVSSELRSLLCCARGRTPPSLGPQDESCTTASSSLAKDTSS
(Seq. ID No. 1)

B. Amino acid sequence of the wild-type β 2AR

MGQPGNGSAFLAPNRSHAPDHDTQQRDEVWWVGMSGIVMSLIVLAI~~VFGNVL~~
VITAI~~AKFERLQ~~TNYFITSLACADLV~~MGLAVV~~PFGAAHILMKMWTFGNFWC
EFWTSIDVLCVTASIETLCVIAVDRYFAITSPFKYQSLLT~~KNKARVII~~LMVWI
VSGLTSFLPIQMHWYRATHQEAINCYANETCCDFTTNQAYAIASSIVSFYVPL
VIMVFVYSRVFQEAKRQLQ~~KIDKSEGR~~FHVQNLSQVEQDGRTGHGLRRSSKFC
LKEHKALKT~~LG~~I~~IMG~~T~~FTL~~CWL~~PFF~~IVNI~~VHVI~~QDNLIRKEVYILLNWIGYVN
SGFNPLIYCRSPDFRIAFQELLCLRSSLKAY~~GNGYSSNGNT~~GEQSGYHVEQE
KENKLLCEDLPGTEDFVGHQGTVP~~SDNIDSQGRNC~~STND~~SLL~~
(Seq. ID No. 2)

Amino Acid Sequence of the Chimeric Receptors

C. Amino acid sequence of the β 2AR-V2R chimera (Oakley et al.)

MGQPGNGSAFLAPNRSHAPDHDTQQRDEVWWVGMSGIVMSLIVLAI~~VFGNVL~~
VITAI~~AKFERLQ~~TNYFITSLACADLV~~MGLAVV~~PFGAAHILMKMWTFGNFWC
EFWTSIDVLCVTASIETLCVIAVDRYFAITSPFKYQSLLT~~KNKARVII~~LMVWI
VSGLTSFLPIQMHWYRATHQEAINCYANETCCDFTTNQAYAIASSIVSFYVPL
VIMVFVYSRVFQEAKRQLQ~~KIDKSEGR~~FHVQNLSQVEQDGRTGHGLRRSSKFC
LKEHKALKT~~LG~~I~~IMG~~T~~FTL~~CWL~~PFF~~IVNI~~VHVI~~QDNLIRKEVYILLNWIGYVN
SGFNPLIYCRSPDFRIAFQELLCARGRTPPSLGPQDESCTTASSSLAKDTSS
(Seq. ID No. 3)

*shown in bold are the amino acids that were moved to the β 2AR to increase its affinity for arrestin.

Figure 10

A. Amino acid sequence of the MOR-V2R chimera expressed from the pEAarrB-1/MOR vector

MDSSTGPGNTSDCSDPLAQASCSPAPGSWLNLSHVDGQNQSDPCGLNRGLGGN
DSLCPQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIY
IFNLALADALATSTLPPQSVDNYLMGTWPFGTILCKIVISIDYYNMFTSIFTLC
TMSVDRYIAVCHPVKALDFRTPRNAKIVNVNCNWILSSAIGLPVVMFMATTKYRQ
GSIDCTLTFSHPTWYWEVNLKKICVFIFAFIMPILIIITCYGLMILRLKSVRML
SGSKEKDRNLLRIRTRMVLLVVAVFIVCWTPIHIYVIKKALITIPETTFQTVSW
HFICIALGYTNCLNPVLYAFLDENFKRCFREFCAAARGRTPPSLGPQDESCTT
ASSSSLAKDTSS

(Seq. ID No. 4)

B. Amino acid sequence of the D1AR-V2R chimera expressed from the pEAarrB-1/D1AR vector

MAPNTSTMDEAGLPAERDFSFRILTACFLSLLILSTLLGNTLVCAAVIRFRHL
RSKVTVNFFVIVSLAVSDLILVAVLVMPWKAVAEIAGFWPFGFCNIWVAFDIMCS
TASILNLCVISVDRYWAISSPFQYERKMTPKAAFILISVAWTLISLSPFIPVQ
LSWHKAKPTWPLDGNTFSLEDTEDDNCDCTRLSRTYAISSSLISFYIPVAIMIV
TYTSIYRIAQKQIRRIASALERAADVHAKNCQTTAGNGNPVECAQSESSFKMSFK
RETKVLTLSVIMGVFVCCWLPPFISNCMVPFCGSEETQPFICIDSITFDVFVW
FGWANSSLNPVLYAFLNADFQKAFTLLGCYRLCAAARGRTPPSLGPQDESCTT
ASSSSLAKDTSS

(Seq. ID No. 5)

C. Amino acid sequence of the 5HT1AR-V2R chimera expressed from the pEAarrB-1/5HT1AR vector

MDVLSPGQGNNTTSPPAPFETGGNTTGISDVTVSYQVITSLLLGTLLIFCAVLG
NACVVAIAALERSLQN VANYLIGSLAVTDLMVSVLVLPMMAALYQVLNKWTLGQ
VTCDFLFIADVLCTSSILHLCATIALDRYWAITDPIDYVNKRTPRRAAALISL
TWLIGFLISIPPMLGWRTPEDRSDPDACTISKDHGYTIYSTFGAFYIPLLML
VLYGRIFRAARFRIRKTVKKVEKTGADTRHGASPAPQPKKSVNGESGSRNWRL
GVESKAGGALCANGAVRQGDDGALELEVIEVHRVGN SKEHLPLPSEAGPTCAP
ASFERKNERNAEAKRKMALARERKTVKTLGIIMGTFILCWLPFFIVALVLPFC
ESSCHMPTLLGAI

Figure 10 (cont.)

INWLGYNSNLLNPVIYAYFNKDFQNAFKKI I KCNFAAARGRTPPSLGPQDES
CTTASSSSLAKDTSS

(Seq. ID No. 6)

D. Amino acid sequence of the β 3AR-V2R chimera expressed from the pEArrB-1/ β 3AR vector

MAPWPHENSSLAPWPDLPTLAPNTANTSGLPGVPEAALAGALLALAVLATVG
GNLLVIVAIATWPRLQTMTNVFTSAAADLVMGLLVVPPAATLALTGHWPLG
ATGCELWTSVDLVCVTASIETLCALAVDRYLAUTNPLRYGALVTKRCARTAVV
LVWVVAASVAFAPIMSQWWRVGADAEAQRCHSNPRCCAFASNMPYVLLSSSVS
FYLPPLLVLMLFVYARVFVVAATRQLRLRGEGLRFPPPEESPPAPSRLAPAVG
CAPPEGVPACGRRPARLLPLREHRACTLGLIMGTFTLCWLFFFLANVIRALG
GPSLVPGPAPFLALNWLGYANSAFNPLIYCRSPDPFRSAFRRLLCRAAAARGRTP
PSLGQPQDESCTTASSSSLAKDTSS

(Seq. ID No. 7)

E. Amino acid sequence of the Edg1R-V2R chimera expressed from the pEArrB-1/Edg1R vector

MGPTSVPLVKAHRSSVSVDVNYDI I VRHYNYTGKLNI SADKENS I KLT SVVFI
LICCFIILENIFVLLTIWKTKKFHRPMYYFIGNLALS DLLAGVAYTANL LLSG
ATTYKLTPAQWFLREGSMFVALSASVFSLLAIAITERYITMLKMKLHN GSN NFR
LFLLI SACWVISLILGGLPIMGWCN CISALSSCSTVLPLYHKHY I LF CTTVFTL
LLLSIVILYCRYISLVRTRSRRLTFRKNISKASRSSEKSL ALLKTVI I VLSVF
IACWAPLFI LL DVGCKVKTC DIL FRAEYFLVLA VLNSGTNP II YTL TNKEM
RRAFIRIMSCCKCAARGRTPPSLGPQDESCTTASSSSLAKDTSS

(Seq. ID No. 8)

Figure 11

A. Nucleotide sequence of the β 2AR-V2R chimera

Wriggins
(SEQ ID No. 9)

B. Nucleotide sequence of the MQR-V2B chimera

(SEQ ID No. 10)

C. Nucleotide sequence of the D1AR-V2R chimera

ctgtccttatatccttcatcccgactacagctaagctggcacaaggcaagccccatggccctt
ggatggcaattttatccctccggggacaccggggatgacaaactgtgacacaaagggtggcagg
acgttgtccatccatcgccatcatcgatttatcaccccgatccatattatgtcgact
acaccaatgtatccatcaggattgcggcagaagcaaacccggcgcatctcagcccttgagaggcgaga
gtccatggcaaaatgtccggacaccggccatggggaaaccggcgatcgacccggccatgtcc
aaatgtccatggatgtccatccaaaggggagacaaatgtttaaaagcgctgtgtatcat
gggggtgtttgtgtctgtccctttctatctcgactgtatgtgccttctgtgg
tctggaggacaccggccatctcgatcgatccatccctcgatgtgtgtgtgtgg
ggccgaattttccctgcacccatattatgtttatgttgcgtactccatgggg
aacccctttagatgtacagactctgcgcggccgcacggggacgcaccccaacccagcctggg
ccccaaatgtactgtccatccggccagactctccctggccaaaggacacttcatcgta
(SEO ID No. 11)

D. Nucleotide sequence of the 5HT1AR-V2R chimera

atggatgtgtcgtacggccctggtcagggcaacaacaccatcacccaccggctccctttagacacg
ggccaaactactgttatctccgcgtgcgcgtactccatcgatccactctgtgt
ggccacgtctttgtcgccgtgtggcaatgcgtcggtgtggccatcgccgtggag
cgccctgtcagaacgtcgccaaattatcttatggcttgggggtaccgacccatgtgt
cggtgttggtgtcccatggccgcgtgtatcagggtctcaacaactggacactggccagg
aacctgcgtacgttgcgtccctcgacgtcgacccatcatctggacactgtgc
ggccatcgccgtgtggacactggccatcaggacccatcgactacgtgaacaaggaggacgc
cccgccgcgcgcgtgcgtcatctcgctacttgggttattgtgttcctcatctccccc
catgtcggtggccgcaccccgaaagaccgtcgaccggacgtcaccattagcaaggat
catggtcatacatatcttcacccatgggttttacatccccgtgtgtcatgtgttc
tctatgggcgcataatccgcgtcgccgttccgcatccgcgaagacgtcaaaaagggtggagaa
gaccggaggccgcaccccgccatcgacatccgcggcccgccgcggccaaaggatgtgt
gagtccggggaggcaggaaactggcggtgggtggagacaaagggtgggtgtgtgtgcgc
atggccgggtggacaaagggtgcgtggccgcgcgttggagggtatcgagggtcaccgg
caactccaaagacactgtccctcccccggagggtgtgttccactcccttgcccccgcct
ttcgagaggaaaatggcgcacccgcggaggccaaaggacatggccgtggccagagaga
agacatgtgaacgcgtggccatcatgggcacccatctctgtgggtgccttccat
ctgtggctcttgttgccttcggagacgtcgccacatggccaccctgttggggccata
atcaattgggtgggtactcaactctgttgcattaccggccgtcattacgcataacttcaaaagg
atcttcaaaagggtttaaaagatcattaaagtgtaaacttgcgcggccgcacggggacgcac
cccacccaggctgggtccccaaagatgagtctgcaccacccggccagctccctggccaaggac
acttcatcgta
(SEO ID No. 12)

E. Nucleotide sequence of the β 3AR-V2R chimera

tctcttagtccccggcccggtttccttcgcctgaactggctagggtatgccaattctgcctta
acccgcgtatctactgcgcagccggactttcgacgcgcctccgcgttctgtgcgcgt
cgccggccgcacgggacgcacccacccagctgggtccccaagatgagtctgcaccacccgcact
cctccctggcaaggacacttcatcgtga
(SEQ ID No. 13)

F. Nucleotide sequence of the Edg1-V2R chimera

atggggcccacccgcgtcccgctggtaaaggcccacccgcagctcggtctctgactacgtcaact
atgtatcatcgccggattacaactacacggaaactgtaatatacgccggacaaggaga
cagcatataactgcacctcggtgttcatcttcatctgtgtttatcatctggaaacatc
tttgcttgcgaccattggaaaaccaagaataatccacccgaccatgtactatttatggca
atctggcccttcagacactgtggcaggagttagcctacacagctaacctgtttgtgtgggc
caccacataacaactgcactccgcggcactgggtttctggaaaggaggatgttgtgtggccctg
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aactccacacacgggagaataactccgcgccttcgtatcggcgttgcgcactgcgcctgtatcc
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accgtgtgcgcgttaccacaaagactatatacttcgttgcaccacgcgttcaactgttcc
tgcgttccatgttacttcgtcagaatctacttcgttgcaggactcggagccgcgcct
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gcgttgcgttgcaccacccatcatgttgcgttgcgcgttgcgcgttgcgcgttgcgcgtt
tgggtcccaagatgagtgcgttgcaccacccgcagctccctggccaaaggacacttcatcgt
a
(SEQ ID No. 14)

FIGURE 12

β arr2-GFP Translocation to the MOR and MOR-V2R Chimera
in Response to Morphine

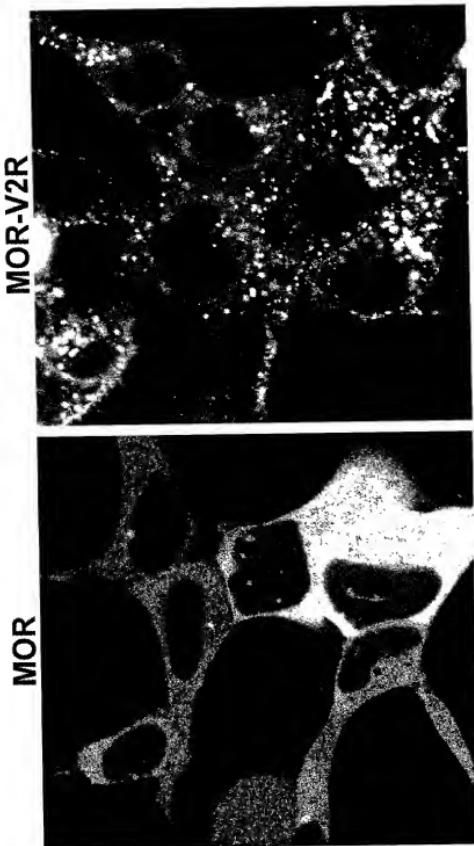


FIGURE 13

β arr2-GFP Translocation to the D1AR and D1AR-V2R Chimera
in Response to Dopamine

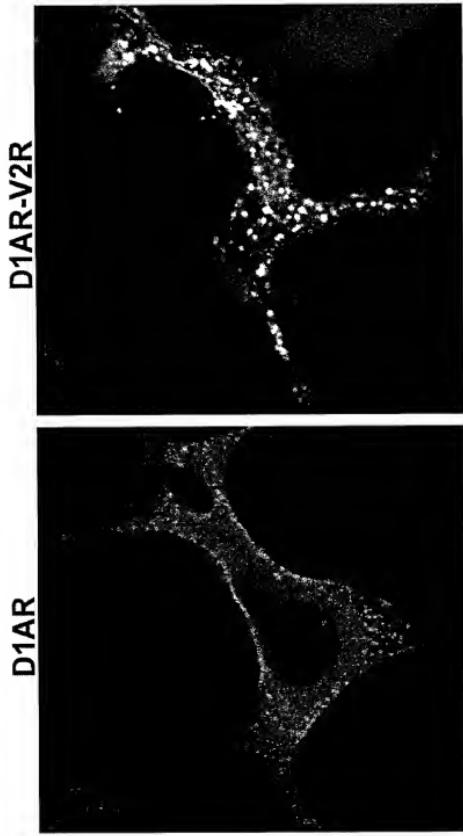
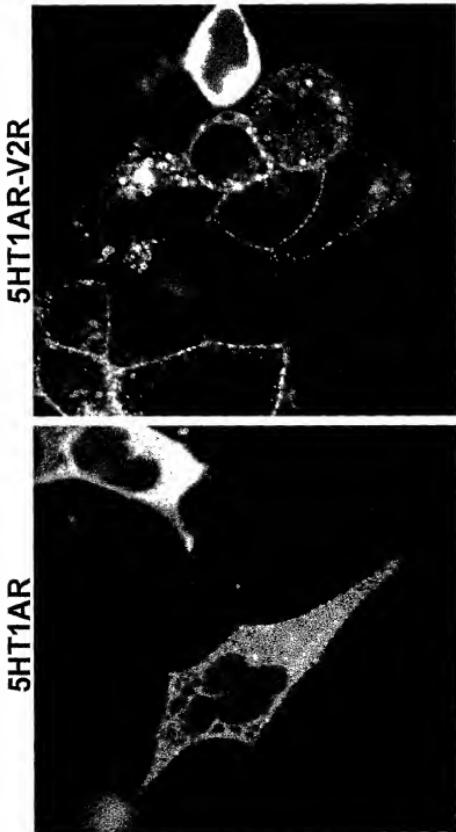


FIGURE 14

β arr2-GFP Translocation to the 5HT1AR and 5HT1AR-V2R
Chimera in Response to Serotonin



**β arr2-GFP Translocation to the β 3AR and β 3AR-V2R Chimera
in Response to Isoproterenol**

FIGURE 15

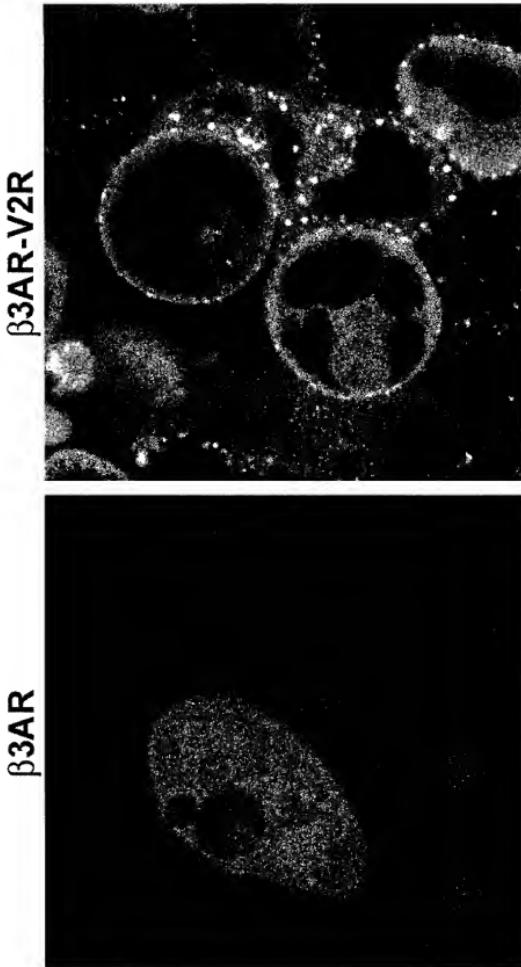


FIGURE 16

β arr2-GFP Translocation to the Edg1 and Edg1-V2R Chimera
in Response to Sphingosine-1-Phosphate

